AMENDMENTS TO THE SPECIFICATION

In the specification, please replace Paragraphs [0145], [0220], [0222], [0224], [0225], [0237], [0238], [0242], [0243], and [0246] with the following revised paragraphs:

Amendments to the specification below are indicated with insertions underlined (e.g., insertion), and deletions struckthrough or in double brackets (e.g., ~~deletion~~ or [[deletion]]):

[0145] Figures 8 and 9 depict a cuvette or sample element 120 for use with any of the various embodiments of the analyte detection system 10 disclosed herein. Alternatively, the sample element 120 may be employed with any suitable analyte detection system. The sample element 120 comprises a sample chamber 200 defined by sample chamber walls ~~202~~ 202a-d. The sample chamber 200 is configured to hold a material sample which may be drawn from a patient, for analysis by the detection system with which the sample element 120 is employed. Alternatively, the sample chamber 200 may be employed to hold other organic or inorganic materials for such analysis.

[0220] In certain other embodiments in which the sample comprises blood, the absorption baseline is defined to be the magnitude of the absorption spectrum at an isosbestic wavelength at which water and a whole blood protein have approximately equal absorptions. In such embodiments, the absorption spectrum is shifted to a selected value at the isosbestic wavelength by adding or subtracting a constant offset value across the entire wavelength spectral data set. In addition, the shifting of the absorption spectrum can be performed nonlinearly (e.g., shifting the portions of the absorption spectrum in different wavelength ranges by different amounts). Shifting the absorption spectrum such that the absorption is set to some value (e.g., 0) at a protein-water isosbestic point preferably helps remove the dependence on ~~hemocrit~~ hematocrit level of the overall spectrum position relative to zero. For samples comprising plasma containing whole blood protein, similar techniques can be applied.

[0222] Such information is very useful in subsequent calculations for compensation of instrument-related pathlength non-linearities. Because the measured absorption of the protein and water are identical at the isosbestic wavelength, the measured absorption at the isosbestic

wavelength is independent of the ratios of the protein concentration and the water concentration (~~hemocrit~~ hematocrit level). At an isosbestic wavelength, for a given sample volume, the same amount of absorption would be observed whether the sample was entirely water, entirely protein, or some combination of the two. The absorption at the isosbestic wavelength is then an indication of the total sample volume, independent of the relative concentrations of water and protein. Therefore, the observed absorption at an isosbestic wavelength is a measure of the pathlength of the sample only. In certain embodiments, the observed absorption at an isosbestic wavelength can be useful for measuring the effective optical pathlength for a sample. As a result, various embodiments of the above-described method may be employed to accurately determine the concentration of analyte(s) of interest in a sample independent of optical pathlength, i.e. without need for prior knowledge of the pathlength and/or without requiring that the sample chamber of the sample element conform closely to a specified or expected pathlength. Additionally, such information can be used in subsequent calculations for compensation of instrument-related pathlength nonlinearities. In certain embodiments, these measurements can be made before or concurrently with absorption measurements in other wavelength ranges.

[0224] The goal of the spectroscopic analysis is to derive the ratio of the analyte volume (for example, glucose volume) to the total blood volume using essentially artifact-free spectra. The blood samples are primarily a mixture of three components: plasma, ~~hemocrit~~ hematocrit soup and glucose as illustrated in Figure 22.

[0225] Certain embodiments of the method are based on knowledge of reference absorption spectra for each of the three components. The protein content of plasma is ignored in pooled-blood embodiments, because it is the same for each blood sample. This is a liberty that can be taken with pooled blood but that cannot be extended to individual blood samples, where additional components will be required. The reference spectra for water (plasma) and the analyte (for example, glucose) can be determined with FTIR measurements. The reference spectra for the ~~hemocrit~~ hematocrit soup can be determined from the differential hemoglobin spectra calculated using the blood data.

[0237] In certain embodiments, the method uses the optical density (OD) for a parallel cuvette, parallel illumination and "delta-function" filter, which can be expressed as:

(1) $OD_i = (c_w\alpha_{wi} + c_h\alpha_{hi} + c_g\alpha_{gi}) \cdot d$

where: d = cuvette path length;
c_w = water volume concentration;
c_h = ~~hemocrit~~ hematocrit volume concentration;
c_g = glucose volume concentration;
α_{wi} = water absorption at wavelength 'i';
α_{hi} = ~~hemocrit~~ hematocrit absorption at wavelength 'i'; and
α_{gi} = glucose absorption at wavelength 'i'.

The absorption of the various components (e.g., α_{wi}, α_{hi}, α_{gi}) at various wavelengths is a property of the components themselves, and can be known or provided to the system for use in the calculation of the analyte concentrations. In various embodiments described below, the blood sample is modeled as a three-component mixture of water, ~~hemocrit~~ hematocrit, and glucose (i.e., $c_w+c_h+c_g=1$). Other embodiments can model the blood sample with more components, fewer components, or different components.

[0238] In certain embodiments, the method uses three two-wavelength sets. The first set is in the wavelength region where water absorption dominates. The second set is in a region where water and ~~hemocrit~~ hematocrit absorptions dominate, and the third set in a region where absorptions from all three components dominate. In certain embodiments, the calculations are based on OD differences of each wavelength pair to reduce or minimize offsets and baseline drift errors. Absorption values for the three components at each of the six wavelengths are shown in Table 1:

Wavelength	α_{wi}	α_{hi}	α_{gi}
1	α_{w1}	0	0
2	α_{w2}	0	0
3	α_{w3}	α_{h3}	0
4	α_{w4}	α_{h4}	0
5	α_{w5}	α_{h5}	α_{g5}
6	α_{w6}	α_{h6}	α_{g6}

[0242] In certain embodiments, the "water free" absorptions at wavelengths 3 and 4 are used to calculate the quantity B which is proportional to the product of the ~~hemocrit~~ hematocrit concentration and path length. The quantity B can be termed the "~~hemocrit~~ hematocrit scaling factor," and can be expressed by the following relation:

$$(14) \quad B = \frac{OD_4' - OD_3'}{\alpha_{h4} - \alpha_{h3}} = c_h d \,.$$

In certain embodiments in which the values of ~~hemocrit~~ hematocrit absorption at the two wavelengths is known or provided to the system, this ratio of the difference of two "water free" OD values with the difference of two reference absorption values for ~~hemocrit~~ hematocrit at the same wavelengths yields a ~~hemocrit~~ hematocrit scaling factor B indicative of the amount of ~~hemocrit~~ hematocrit in the sample.

[0243] By using B and the ~~hemocrit~~ hematocrit absorptions at each wavelength, the "glucose only" OD is calculated in certain embodiments to be expressed by the following relation:

$$(15) \quad OD_i'' = OD_i' - B\alpha_{hi} \,.$$

In this way, the "glucose only" OD value equals the measured OD value minus the scaled reference absorption values for water and for ~~hemocrit~~ hematocrit.

[0246] The desired ratio of glucose volume to total blood volume can then be expressed (using the relation $c_w+c_h+c_g=1$) by the following relation:

$$(19) \quad [[C_g = \frac{c_g}{c_w + c_h} = \frac{C}{A+B}]] \underline{C_g = \frac{c_g * d}{(c_w + c_h + c_g) * d} = \frac{C}{A+B+C}} \,.$$

By taking the ratio of the glucose scaling factor to the sum of the water scaling factor, the ~~hemocrit~~ hematocrit scaling factor, and the glucose scaling factor, the resulting concentration ratio c_g is substantially independent of the path length of the sample. Thus, certain embodiments described herein provide a method of determining the glucose content of a blood sample independent of the path length of the blood sample.